IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) A method for determining if a human subject having an estrogen receptor-positive breast cancer has a high risk of relapse or a low risk of relapse following adjuvant ~~predicting the responsiveness of a human subject with breast cancer to a~~ therapeutic treatment, comprising:

obtaining, prior to or during adjuvant therapeutic treatment of a human subject having an estrogen receptor-positive breast cancer, a biological sample comprising breast cancer cell genomic DNA from the subject, wherein the adjuvant therapeutic treatment comprises treatment with one or~~of~~ more drugs that inhibit~~target~~ the estrogen receptor pathway of breast cancer cells~~or that are involved in estrogen metabolism, production or secretion~~; and

determining the genomic DNA methylation status of at least one CpG dinucleotide of at least one target nucleic acid sequence of the PITX2 gene, and the regulatory regions thereof selected from the group consisting ~~essentially~~ of SEQ ID NO:83, complements thereof, and contiguous portions thereof, by contacting the at least one target nucleic acid sequence with one or more agents suitable to convert cytosine bases that are unmethylated at the 5'-position thereof to a base that is detectably dissimilar to cytosine in terms of hybridisation properties, wherein hypomethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative of~~for~~ a low risk for relapse following adjuvant therapeutic treatment and ~~while~~ hypermethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative of~~for~~ a high risk for relapse following adjuvant therapeutic treatment~~, wherein predicting responsiveness of the subject to the adjuvant therapeutic treatment is afforded~~.

2.-19. (Cancelled)

20. (Currently amended) The method of claim 1, wherein said breast cancer is selected from the group consisting ~~essentially~~ of ductal carcinoma in situ, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma

in situ, lobular carcinoma in situ and papillary carcinoma in situ.

21. (Previously presented) The method of claim 1, wherein said subject is also progesterone receptor positive.

22. (Previously presented) The method of claim 1, wherein said therapeutic treatment is for the treatment of a relapse or metastatic breast cancer.

23. (Cancelled)

24. (Previously presented) The method of claim 1, wherein said subject did not receive a chemotherapeutic treatment.

25.-44. (Cancelled)

45. (Currently amended) A method for determining if a human subject having an estrogen receptor-positive breast cancer has a high risk of relapse or a low risk of relapse following adjuvant ~~predicting the responsiveness of a human subject with breast cancer to a~~ therapeutic treatment, comprising:

obtaining, prior to or during adjuvant therapeutic treatment of a human subject having estrogen receptor-positive breast cancer, a biological sample comprising breast cancer cell genomic DNA from the subject, wherein the adjuvant therapeutic treatment comprises treatment with one or~~of~~ more drugs that inhibit~~target~~ the estrogen receptor pathway of breast cancer cells~~or that are involved in estrogen metabolism, production or secretion~~;

isolating the genomic DNA;

contacting the isolated genomic DNA, or a portion thereof, with an agent or combination of agents suitable to convert cytosine bases that are unmethylated at the 5-position to uracil, or to another base which is dissimilar to cytosine in terms of base pairing behavior, to provide a pretreated DNA;

amplifying at least one pretreated DNA sequence, or a portion thereof, selected from the sequence group consisting ~~essentially~~ of SEQ ID NOS:411, 412, 685, 686, complements thereof, and contiguous portions thereof; and

determining, based on the amplification or on analysis of amplificates generated by the

amplification, the methylation status of one or more genomic CpG dinucleotide sequences of SEQ ID NO:83, wherein hypomethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative of~~for~~ a low risk for relapse following adjuvant therapeutic treatment and ~~while~~ hypermethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative of~~for~~ a high risk for relapse following adjuvant therapeutic treatment~~, wherein predicting responsiveness of the subject to the adjuvant therapeutic treatment is afforded~~.

46.-56. (Cancelled)

57. (Previously presented) The method of claim 45, wherein determining the methylation status comprises sequencing.

58. (Previously presented) The method of claim 45, wherein amplifying comprises using methylation-specific primers.

59. (Currently amended) The method of claim 45, wherein amplifying comprises use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting ~~essentially~~ of SEQ ID NOS:411, 412, 685, 686, complements thereof, and contiguous portions thereof, wherein said at least one nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of a nucleic acid to which it is hybridized.

60. (Cancelled)

61. (Previously presented) The method of claim 45, wherein contacting is with an agent, or combination of agents, comprising at least on one of bisulfite, hydrogen sulfite and disulfite.

62. (Currently amended) A method for determining if a human subject having an estrogen receptor-positive breast cancer has a high risk of relapse or a low risk of relapse following adjuvant ~~predicting the responsiveness of a human subject with breast cancer to a~~ therapeutic treatment, comprising:

obtaining, prior to or during adjuvant therapeutic treatment of a human subject having

estrogen receptor-positive breast cancer, a biological sample comprising breast cancer cell genomic DNA from the subject, wherein the adjuvant therapeutic treatment comprises treatment with one orof more drugs that inhibittarget the estrogen receptor pathway of breast cancer cellsor ~~that are involved in estrogen metabolism, production or secretion~~;

isolating the genomic DNA;

digesting the isolated genomic DNA, or a portion thereof, comprising at least one sequence selected from the sequence group consisting ~~essentially~~ of SEQ ID NO:83, complements thereof, and contiguous portions thereof, with one or more methylation-sensitive restriction enzymes; and

determining the DNA fragments generated or not generated, wherein the methylation status of a least one CpG dinucleotide of said at least one sequence is determined, wherein hypomethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative offor a low risk for relapse following adjuvant therapeutic treatment and ~~while~~ hypermethylation of SEQ ID NO:83, complements thereof, and contiguous portions thereof is indicative offor a high risk for relapse following adjuvant therapeutic treatment~~, wherein predicting responsiveness of the subject to the adjuvant therapeutic treatment is afforded~~.

63.-66. (Cancelled)

67. (Previously presented) The method of claim 62, further comprising, prior to determining the DNA fragments, amplifying the DNA fragments generated.

68.-76. (Cancelled)

77. (Currently amended) The method of any one of claims 45 and 62, wherein the biological sample containing genomic DNA is obtained from a source selected from the group consisting ~~essentially~~ of cells or cellular components which contain DNA, cell lines, histological slides, biopsies, tissue embedded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, bone marrow, and combinations thereof.

78.-80. (Cancelled)